

**EXHIBIT A**



## FACSIMILE COVER SHEET

Technology Center 1600/2900

DATE: 01/21/03ATTN: Mr. Bruce HamburgFax Number: (212) 953 7733FROM: Isis Ghali

Fax Number:

NUMBER OF PAGES 8 INCLUDING THIS PAGE.

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CONTACT Isis Ghali AT (703) 305 4048

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PTO GROUP 1200



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/503,907	05/24/2000	RAINER HOFFMANN		3754

7590 06/10/2002

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122 EAST 42ND STREET  
NEW YORK, NY 10168

EXAMINER

GHALL, ISIS A D

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 06/10/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

01/21/03 TUE 12:41 FAX 703 30 924

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<b>Office Action Summary</b>	Application No.	Applicant(s)	
	08/508,907	HOFFMANN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(e). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(e).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 February 2002.
- 2a) ☒ This action is FINAL.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 935 O.G. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 and 16-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14, 16-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-848)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

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### DETAILED ACTION

The receipt is acknowledged of applicants' amendment A, and request for extension of time, both filed 2/12/2002.

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Claim 15 has been canceled and claims 17-30 have been added per applicant's amendment A, in Paper No. 8.

Claims 1-14, and 16-30 are included in the prosecution.

The following new rejection is necessitated by applicants' amendment A:

#### ***Claim Rejections - 35 USC § 112***

1. Claims 4, 6 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are confusing because applicants' amendments omit C<sub>7</sub> sulfonic acids from claim 1, while claims 4, 6 and 23 recite C<sub>7</sub> sulfonic acids. Clarification is requested.

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***Response to Arguments***

2. Applicant's arguments filed 2/12/2002 have been fully considered but they are not persuasive.

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**Claim Rejections - 35 USC § 103:**

Claims 1-14, 16-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '539 or US '297.

Both references disclose opioid containing pharmaceutical composition which as useful in effecting transdermal delivery of therapeutic doses of opioid to systemic circulation of mammal. The references disclosed composition comprising opioid as morphine or its acidic salts such as sulfonates, polyethylene glycol and oleic acid. The structure of morphine is inherent. The composition can be in the form of cream, lotion or patch. See US '539 abstract; col.1, lines 60-65; col.2, lines 18-34; col.3, lines 37-38; col.4, lines 2-23. See US '297 abstract; col.1, lines 22-64; col.4, lines 62-63.

However the references do not disclose all the claimed salts of morphine.

Absence of showing criticality or superior and unexpected results of the particular claimed salts render the claims obvious over the prior art.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to produce transdermal composition comprising any of the claimed opioid salts with reasonable expectation of success of the delivered composition in relieving pain.

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**Applicants' Arguments:**

- The references recite the tosylates and applicants are omitting them. Applicants are referring to Figure 4 to which have been added comparison examples 4-6.
  - The references disclosed permeation enhancer in the composition.
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**Examiner's Position:**

- Applicants' claims still recite tosylates in claims 4, 6 and 23. However, it is within the skill in the art to select species when the genus is disclosed recognizing the suitability for the intended purpose. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Ibozek*, 163 USPQ 545 (CCPA 1969). In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been obvious within the meaning of 35 U.S.C. 103 (a). The examiner has not received the appended Fig. 4 that applicants are referring to. Referring to the original Figure 4, applicants' examples 1 and 8 show low flux rate, not significantly higher than the tosylates disclosed by the prior art.
- The expression "comprising" permits the presence of other ingredients, such as permeation enhancers, and does not preclude the presence of other ingredients,

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active or inactive, even in major amounts. See *Moleculon Research Corporation v CBS, Inc.* 229 USPQ 805, *In re Baxter* 210 USPQ 795, 803.

### Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 6,156,764 disclosed morphine salts of anionic narcotic analgesics of the substituted carboxylic acid. US 6,150,524 disclosed morphine derivatives with analgesic activity.

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5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Isis Ghali  
Examiner  
Art Unit 1615

  
THURMAN K. PAGE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600